The opinion support of the decision being entered toda as <u>not</u> written for publication and is <u>not</u> binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte RAFAEL ARGUELLO, and ALEJANDRO MADRIGAL

Application No. 09/077,615

ON BRIEF

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U.S. PATENT AND TRADEMARK OFFICE BOARD OF PATENT APPEALS AND INTERFERENCES

Before WINTERS, ADAMS and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 55-69 and 73-76, which are all the claims pending in the application.

Claim 55 is illustrative of the subject matter on appeal and is reproduced below:

- 55. A method for identifying a DNA molecule comprising:
 - (a) hybridizing a single strand DNA molecule with a complementary reference DNA strand to form a test duplex;
 - (b) separating the test duplex from at least one control duplex run in the same separation;
 - (c) detecting the positions to which the test duplex and the at least one control duplex migrate in the separation;
 - (d) assigning an exact numerical migration value to the position to which the test duplex migrates; and

(e) identifying the DNA molecule by matching the exact migration value with a database of migration values of identified DNA molecules, wherein the database of migration values is independent of the separation.

The references relied upon by the examiner are:

Mullins et al. (Mullins)

WO 95/01453

Jan. 12, 1995

Sapirstein et al. (Sapirstein), "Computer-aided wheat cultivar identification and analysis of densitometric scanning profiles of gliadin electrophoregrams," <u>Seed Sci. & Technol.</u>, Vol. 14, pp. 489-517 (1986)

Zimmerman et al. (Zimmerman), "Exploiting structural differences among heteroduplex molecules to simplify genotyping the DQA1 and DQB1 alleles in human lymphocyte typing," <u>Nucleic Acids Res.</u>, Vol. 21, No. 19, pp. 4541-4547 (1993)

GROUNDS OF REJECTION

Claims 55-69 and 73-76 stand rejected under 35 U.S.C. § 103 as being unpatentable over Zimmerman in view of Sapirstein.

Claims 55-69 and 73-76 stand rejected under 35 U.S.C. § 103 as being unpatentable over Zimmerman, in view of Sapirstein and Mullins.

We reverse.

DISCUSSION

Zimmerman in view of Sapirstein:

As we understand the examiner's argument (Answer, pages 3-5),

Zimmerman teach every aspect of appellants' claimed invention except
assigning an exact numerical migration value to the position to which the test
duplex migrates (e.g., claim 55, step (d)), and identifying the DNA molecule by
matching the exact migration value with a database of migration values of
identified DNA molecules, wherein the database of migration values is

independent of the separation (e.g., claim 55, step (e)). The examiner relies on Sapirstein to make up for this deficiency in Zimmerman. According to the examiner (Answer, page 5), Sapirstein

teach methods which comprise separating [wheat gliadin] proteins from one another and from control proteins, detecting the positions to which the test proteins and ... at least one control protein migrates in the separation, assigning an exact numerical migration value to the position to which the test proteins migrate[], and identifying the protein pattern by matching the migration value with a database of migration values of protein patterns (p. 492-496). Especially pertinent in this analysis is the fact that Sapirstein et al. teach methods for determining band migration distances and relative mobilities of species in an electrophoresis gel and a database for the comparison of such mobility values for the identification of a test sample.

Based on this evidence, the examiner finds (id.), it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made "to have assigned exact numerical migration values to the movement of heteroduplexes in the methods taught by Zimmerman et al., and to have included these values in a database, as is exemplified by the teachings of Sapirstein et al. for a different test system." According to the examiner (id.), a person of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to take advantage of the benefits of the database type analysis taught by Sapirstein which include the precision obtained "compared to manual measurement procedures using rules or microcomparators," the speed of the analysis resulting from computerization, and "the facility to compare and manipulate normalised gliadin PAGE pattern using computer graphics...."

According to the examiner (Answer, bridging paragraph, pages 5-6), the analytic methods taught by Sapirstein can be applied to Zimmerman because Zimmerman teach that

"identifying novel alleles is based on positive detection of HD [(heteroduplex)] products with unique electrophoretic mobilities (p. 4545)." Thus the ordinary practitioner would have been motivated to use a measurement method such as the ones taught by Sapirstein et al. in order to have provided a clear and quantitative methodology for allele identification.

For their part, appellants argue (Brief, page 5, alteration original), the combination of Zimmerman and Sapirstein

fail to teach or suggest at least two steps of the claimed invention, namely "assigning an exact numerical migration value to the position to which the test duplex migrates[,]" and "identifying the DNA molecule by matching the exact migration value with a database of migration values of identified DNA molecules, wherein the database of migration values is independent of the separation."

According to appellants (<u>id.</u>), the examiner admits Zimmerman does not "assign an exact numerical migration value to the distance traveled by the heteroduplexes," or "provide a database of migration values of identified DNA molecules as required by the instant claims." In addition, appellants assert (Brief, page 6), Sapirstein fails to make up for the deficiencies in Zimmerman, because Sapirstein "only care about protein banding patterns, not the identity of any specific protein in the banding pattern." As appellants explain (Brief, bridging paragraph, pages 4-5), Sapirstein

do not disclose identification of anything at the molecular level, such as protein or DNA. ... In simplistic terms, [Sapirstein teach] if

¹ <u>See also</u> Answer, page 13, wherein the examiner states "[t]he examiner and appellant agree that Zimmerman et al. fail to teach steps (d) and (e) of the claim."

the banding pattern of sample X matches the database banding pattern for cultivar Y, then sample X is cultivar Y. The identity or sequence of the specific proteins that make up the banding pattern are irrelevant.

The examiner disagrees with appellants' characterization of Sapirstein.

According to the examiner (Answer, page 13), Sapirstein exemplify

"the fact that electrophoretic mobilities have been used in a fashion wherein they are stored in a database as exact numerical values and called up for later comparison and identification." Thus, the examiner asserts (id.), "underlying Sapirstein et al.'s methodology is the assumption that the same proteins will migrate to the same places, and differences in protein compositions among cultivars will allow their identification."

As set forth in <u>In re Kotzab</u>, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. ... Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher."

Most if not all inventions arise from a combination of old elements. ... Thus, every element of a claimed invention may often be found in the prior art. ... However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. ... Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. [Citations omitted].

In other words, "there still must be evidence that 'a skilled artisan, ... with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." <u>Ecolochem Inc. v. Southern California Edison</u>, 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075-76 (Fed. Cir. 2000).

As we understand the evidence of record, Sapirstein teach the use of computerized methods for calculating and storing data regarding the migration values, stated differently the migration pattern, of a plurality wheat gliadin proteins which can then be used to determine the identity of an unknown wheat cultivar. In contrast, Zimmerman teach a method of exploiting unique electrophoretic mobilities, due to structural differences among heteroduplex molecules, to identify polymorphisms in the second exon of major histocompatibility complex class II sequences. According to the examiner (Answer, page 6), a person of ordinary skill in the art at the time the invention was made would have been motivated to modify the method of Zimmerman with the teachings of Sapirstein, in order to obtain "a clear and quantitative methodology for allele identification."

While the examiner has, at best, established that individual parts of the claimed invention were known in the prior art, we are compelled to find that the evidence of record fails to suggest the combination set forth by the examiner.

While a person of ordinary skill in the art may possess the requisite knowledge and ability to modify the protocol taught by Zimmerman, the modification is not obvious unless the prior art suggested the desirability of the

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modification. In re Gordon, 733 F.2d 900, 902, 211 USPQ 1125, 1127 (Fed. Cir. 1984). Here we see no reason to modify the references as applied. As appellants point out (Brief, page 7, emphasis removed), Zimmerman's heteroduplex "pattern is comprised of a single product in homozygous individuals or two products in heterozygous individuals...." Thus, appellants note (id.), Zimmerman "repeatedly point out that their method is simple and provides results that are easy to interpret." In contrast to the "simple" method taught by Zimmerman, Sapirstein teach the use of specialized computer aided techniques to measure and compare wheat gliadin protein banding patterns, due in part to "the unusual complexity of the gliadin electrophoregram itself." See Sapirstein, page 491, lines 6-9. Thus, Zimmerman and Sapirstein differ not only is the starting material used, and the result obtained (e.g., identification of a specific allele in Zimmerman, versus identification of a specific type of wheat cultivar in Sapirstein), they also differ in the complexity of the migration patterns obtained (e.g., one or two in Zimmerman versus Sapirstein's unusually complex electrophoregram).

On reflection, we find no reasonable suggestion for combining the teachings of the references relied upon by the examiner in a manner that would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. The initial burden of presenting a <u>prima facie</u> case of obviousness rests on the examiner. <u>In re Oetiker</u>, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On these circumstances, we are constrained to reach

the conclusion that the examiner has failed to provide the evidence necessary to support a prima facie case of obviousness.

Accordingly, we reverse the rejection of claims 55-69 and 73-76 under 35 U.S.C. § 103 as being unpatentable over Zimmerman in view of Sapirstein.

Zimmerman, in view of Sapirstein and Mullins:

The examiner relies on Zimmerman and Sapirstein as set forth above.

According to the examiner (Answer, page 14), Mullins "exemplify the calculation of migration distances for single DNA duplexes on page 21 and figure 8." Based on this evidence, the examiner concludes (Answer, page 9),

[i]t would have been <u>prima facie</u> obvious to one of ordinary skill in the art at the time the invention was made to have assigned exact numerical migration values to the movement of heteroduplexes in the methods taught by Zimmerman <u>et al.</u> using the methodology provided by Mullins <u>et al.</u>, and to have included these values in a database, as is exemplified by the teachings of Sapirstein <u>et al.</u> for a different test system.

In response, appellants assert (Brief, page 9), like Sapirstein, Mullins "is simply not capable of providing for the positive and actual identification of any of the DNA molecules in the heteroduplex bands as is required by the claimed invention." The examiner does not dispute this assertion. Instead, the examiner asserts (Answer, page 9), Mullins was "included in this rejection merely to demonstrate that it was known in the art at the time the invention was made to determine exact numerical mobility values for heteroduplex nucleic acid molecules." Conspicuous by its absence, however, is any statement by the

examiner as to where the prior art would have suggested the combination of Mullins with Zimmerman and Sapirstein.

The initial burden of presenting a <u>prima facie</u> case of obviousness rests on the examiner. <u>Oetiker</u>. On this record, we find no reasonable suggestion for combining the teachings of the references relied upon by the examiner in a manner that would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. On these circumstances, we are constrained to reach the conclusion that the examiner has failed to provide the evidence necessary to support a prima <u>facie</u> case of obviousness.

Accordingly, we reverse the rejection of claims 55-69 and 73-76 under 35 U.S.C. § 103 as being unpatentable over Zimmerman in view of Sapirstein and Mullins.

REVERSED

Sherman D. Winters
Administrative Patent Judge

Jell & frame

BOARD OF PATENT

Donald E. Adams

Administrative Patent Judge

APPEALS AND

INTERFERENCES

Lora M. Green

Administrative Patent Judge

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